

REMARKS

INTRODUCUTORY MATTER

The present application is a continuation of International PCT Application No. PCT/US00/15248 filed June 2, 2000. The specific amendments to the specification and original claim 2 of the present application are further discussed below in detail. Pursuant to 37 C.F.R. § 1.121(b)(iii), applicants submit a marked up version of the amended paragraphs on pages 26 and 28 (see, Appendix I). Pursuant to 37 C.F.R. §1.121(c)(ii), applicants have enclosed a marked up version of amended claim 2 (see, Appendix II).

None of the above amendments adds any new matter.

THE AMENDMENTS

In the Specification

Applicants submit substitute paragraphs for original paragraphs found on page 26, lines 8-17 and page 28, lines 6-23, which have been amended to incorporate the sequence identifiers pursuant to 37 C.F.R. §1.821 (d).

Claim 2

Original claim 2 referred to compounds depicted in the specification. Applicants have amended original claim 2 to recite the compounds of Table 1 within the claim as amended.

CONCLUSION

Applicants request that the Examiner consider the foregoing remarks and enter the indicated amendments prior to substantive examination of this application.

Respectfully submitted,



Andrea L. C. Robidoux (Reg. No. 47,902)
Agent for Applicants
c/o Vertex Pharmaceuticals Inc.
130 Waverly St.
Cambridge, MA 02139-4242
Tel: (617) 444-6731



APPENDIX I

Replacement paragraph (page 26, lines 8-17):

The construct was prepared by PCR using deoxyoligonucleotides

5' GCTCTAGAGCTCCATGGGCAGCAAAAGCAAAGTTGACAA 3' [SEQ ID NO: 1] (forward primer with initiation codon underlined) and 5' TAGCGGATCCTCATTCTGAATTCATTACTTCCTTGTA 3' [SEQ ID NO: 2] (reverse primer with stop codon underlined)

as primers and was confirmed by DNA sequencing. Control experiments indicated that the truncated JNK3 protein had an equivalent kinase activity towards myelin basic protein when activated with an upstream kinase MKK7 *in vitro*.

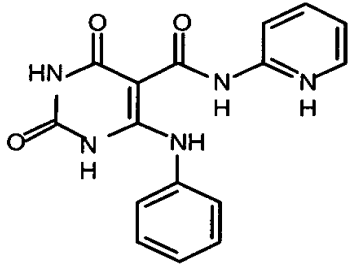
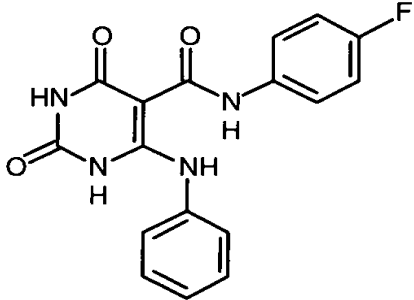
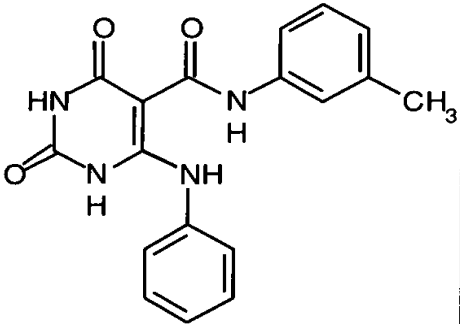
Replacement paragraph (page 28, lines 6-23):

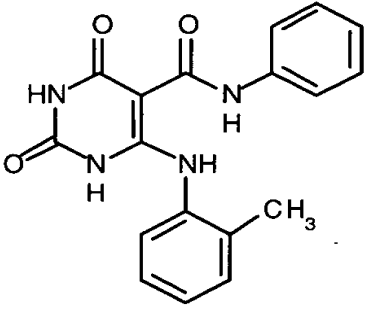
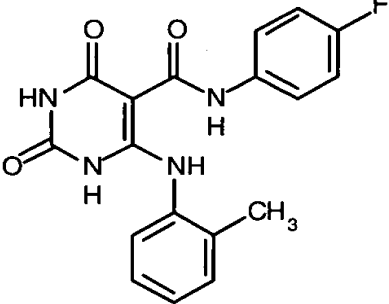
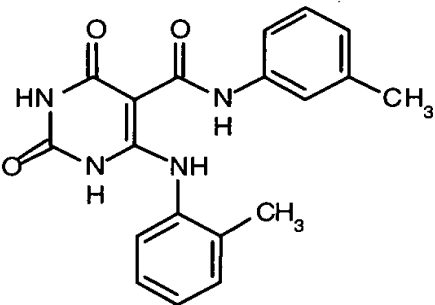
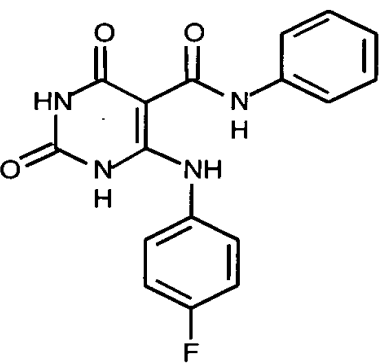
Compounds were assayed for the inhibition of JNK3 by a spectrophotometric coupled-enzyme assay. In this assay, a fixed concentration of activated JNK3 (10 nM) was incubated with various concentrations of a potential inhibitor dissolved in DMSO for 10 minutes at 30°C in a buffer containing 0.1 M HEPES buffer, pH 7.5, containing 10 mM MgCl₂, 2.5 mM phosphoenolpyruvate, 200 μM NADH, 150 μg/mL pyruvate kinase, 50 μg/mL lactate dehydrogenase, and 200 μM EGF receptor peptide. The EGF receptor peptide has the sequence KRELVEPLTPSGEAPNQALLR [SEQ ID NO: 3], and is a phosphoryl acceptor in the JNK3-catalyzed kinase reaction. The reaction was initiated by the addition of 10 μM ATP and the assay plate is inserted into the spectrophotometer's assay plate compartment that was maintained at 30°C. The decrease of absorbance at 340 nm was monitored as a function of time. The rate data as a function of inhibitor concentration was fitted to competitive inhibition kinetic model to determine the K_i.

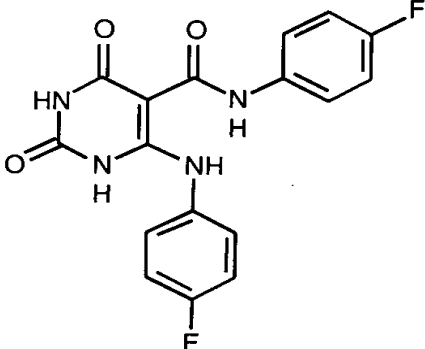
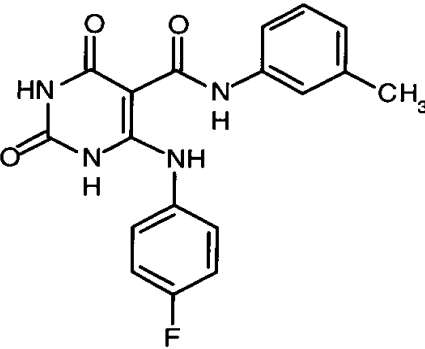
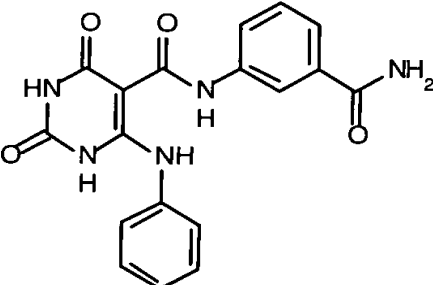


Appendix II

Claim 2. (Amended) The compound according to claim 1, wherein the compound is selected from any one of [the compounds depicted in Table 1.] the following compounds:

<u>Cmpd</u>	<u>Structure</u>
<u>2</u>	
<u>3</u>	
<u>4</u>	

5	
6	
7	
8	

<u>9</u>	 <chem>O=C1NC(=O)C(Nc2ccc(F)cc2)=C(NC(=O)c3ccc(F)cc3)N1</chem>
<u>10</u>	 <chem>CC1=CC=C(NC(=O)c2ccc(F)cc2)C(=O)N1C(=O)Nc3ccc(C)cc3</chem>
<u>11</u>	 <chem>NC(=O)c1ccc(NC(=O)c2c(NC(=O)N3C(=O)NC(=O)N3)cc4ccccc42)cc1</chem>